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10/520,078	04/04/2005	Jamila Najib	BJS-3665-126	9205

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EXAMINER	
ZAREK, PAUL E	
ART UNIT	PAPER NUMBER
4161	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,078	NAJIB ET AL.	
	Examiner	Art Unit	
	PAUL ZAREK	4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-68* is/are pending in the application.

4a) Of the above claim(s) *61,62 and 68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-60 and 63-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/05/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-37 have been canceled by the Applicant. Claim 38-68 were added on 02/05/2005. Claims 38-68 are currently pending. This is the first Office Action on the merits of the claim(s).

Election/Restrictions

2. Applicant's election without traverse of Group II (Claims 38-60 and 63-67) in the reply filed on 07/28/2008 is acknowledged. Claims 62 and 68 are withdrawn as being drawn to a non-elected Group.

3. Applicant's election without traverse of Compound 29 (1-[4-methylthiophenyl]-3-[3,5-dimethyl-4-carboxydimethylmethyloxyphenyl]prop-2-en-1-one) in the reply filed on 07/28/2008 is acknowledged. After an extensive search, the elected compound was found free of the prior art. Examiner moved onto the next derivative of formula I, 4'-carboxyethoxy-4-sulphochalcone, wherein:

X_1 = -G_1R_1, wherein G_1 is -O and R_1 is -$CH_2CH_2COOR_6$ (group 1), wherein R_6 is –H;
X_2 = -H;
X_3 = -R_3, wherein R_3 is –H;
X_4 = -SO_3H; and,
X_5 = -R_5, wherein R_5 is-H; and,
X_6 = -O

Applicant is reminded that upon allowance of a generic claim, Applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise

include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. Claims 38-40, 42, 44, 46-48, 56, 58, 63-65, and 67 read on examined species. Claims 41, 43, 45, 49-55, 57, 59-62, and 66 are withdrawn as being drawn to a non-examined species.

Priority

4. Applicant's claim for the benefit of a prior-filed international application, PCT/FR/03/02128 (filed on 07/08/2003) under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The effective filing date for the instant application is 07/08/2003.

5. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy for French patent application 0208570 (filed on 07/08/2002) has been filed. The foreign priority date for the instant application is 07/08/2002.

Claim Objections

6. Claims 38 and 39 are objected to because of the following informalities: The structure disclosed for formula I has a bond linking X_2 to C3 of the propenyl chain between the phenol rings. Since X_2 is -H, any bond between C3 and X_2 is not permitted. Appropriate correction is required.

Claim Rejections - 35 USC § 112 (1st paragraph)

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 38-60 and 63-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds of formula I, optical and geometric isomers, racemates, tautomers, and salts thereof, does not reasonably provide enablement for hydrates of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

9. In the case In re Wands', 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have need described. They are:

1. the nature of the invention;
2. the state of the prior art;
3. the predictability or lack thereof in the art
4. the amount of direction or guidance present;
5. the presence or absence of working examples;
6. the breadth of the claims;
7. the quantity of experimentation needed; and,
8. the level of the skill in the art.

Claims 38-60 and 63-67 are drawn to compounds of formula (I), as well as optical and geometric isomers, racemates, tautomers, salts, hydrates, and mixtures thereof. According to Byrn, et al. (Solid State Chemistry of Drugs, 1999), "[t]he occurrence of hydrated or solvated crystal forms, crystals in which solvent molecules occupy regular positions in the crystal structure, is widespread but by no means universal among drug substances." (pg 232, emphasis added). Most drug crystals that fall into the category of solvates are hydrates (pg 236).

While the level of skill in pharmacology and organic chemistry is exceedingly high, there is no absolute predictability as to which solvates and/or hydrates will function as intended. Byrn

notes that the water molecule is particularly suited to fill structural voids, due to its small size. In hydrated crystal structures, water molecules bind to other water molecules but also to any available functional group, i.e. carbonyls, amines, alcohols, and many others which are capable of accepting or donating an active hydrogen atom to form hydrogen bonds (pg 236, "Hydrates"). Also, the behavior of hydrates of pharmaceuticals is unpredictable due to dehydration prior to melting, and cracking during dehydration (pg 234). Also hydrates and solvates may only be formed under certain conditions, dependent upon the compounds sought to be crystallized. Such a process is not a given in pharmacology and requires a great deal of research, with no guarantee of success.

Furthermore, the stability of solvates and hydrates is not altogether predictable, wherein said stability directly affects the properties of a given molecule. This lack of stability means a hydrate or solvate, if found to possess similar properties as the target compound, may not function as intended in vivo. Such facts lead to the conclusion that more that a mere recitation is needed in order to support a claim to solvates and hydrates. Creating functional solvates and hydrates with the same properties as the mother-compound is by no means routine, thus there must be a showing sufficient to satisfy the enablement requirement.

In the instant case, the Specification provides no guidance as to particular hydrates of formula I. There are no examples given that Applicant has determined the necessary solvents for even one of the thousands of compounds encompassed by the genus that is formula I. There are no determinations as to whether and which hydrates or solvates would function as intended, as useful in the treatment of inflammation, neurodegeneration, deregulation of lipid and/or glucose metabolism, cell proliferation and/or differentiation and/or skin or central nervous system aging.

The level of difficulty required to produce functional hydrates and solvates is extremely high. The level of skill in pharmacology/organic chemistry is also very high. However, despite such a high level of skill in the requisite art, the creation of hydrates and solvates is unpredictable to the extent that undue experimentation is required in order to make and use hydrates and solvates of the claimed compounds. There is an insufficient guidance in the instant specification, and the state of the art does not make up for this deficit. Undue and unpredictable experimentation would be required to make and use the rejected claims commensurate with the scope of the specification. Therefore, instant Specification does not enable one of ordinary skill in the art to make and use the invention commensurate in scope with the claims. Applicant may overcome this rejection by deleting "hydrates" from the language of Claims 38-60 and 63-67.

10. Claims 38-67 are rejected under 35 U.S.C. 112, first paragraph. The instant specification is not enabled either for the treatment or prophylaxis of any pathology associated with inflammation, neurodegeneration, deregulation of lipid and/or glucose metabolism, cell proliferation and/or differentiation and/or skin or central nervous system aging. Therefore, the Specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims.

Many factors are considered when determining whether the evidence is sufficient to satisfy the enablement requirement and whether any necessary experimentation is "undue." In re Wands, 858 F.2d 731, 742 (Fed. Cir. 1988). These factors include, but are not limited to:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Claims 38-67 are drawn to a pharmaceutical composition for the treatment or prophylaxis of any pathology related to inflammation, neurodegeneration, deregulation of lipid and/or glucose metabolism, cell proliferation and/or differentiation and/or skin or central nervous system aging. This claim encompasses both treating and preventing any known and unknown pathology.

The level of ordinary skill in the art is extremely high, with many of the pharmaceutical sciences possessing advanced degrees. Despite the high level of ordinary skill required in pharmacology, Applicant's Specification does not enable Claims 38-67. There is no absolute predictability even in view of the seemingly high level of skill in the art.

The state of the prior art is such that screening *in vitro* and *in vivo* is necessary to determine which compounds exhibit desired pharmacological activities, in this case treatment or prophylaxis of any pathology related to inflammation, neurodegeneration, deregulation of lipid and/or glucose metabolism, cell proliferation and/or differentiation and/or skin or central nervous system aging. The existence of these screening obstacles and nature of the unpredictability of pharmacological arts would prevent one of ordinary skill in the art from accepting a preventive regimen on its face and from accepting the prevention and treatment of these pathologies.

The Applicant provides evidence of the claimed compounds' antioxidant properties, PPAR agonist properties, neuroprotection properties, and anti-inflammatory properties in various *in vitro* and *in vivo* models, however, not all the compounds treated are efficacious. For example, in figure 2-5, compounds 31 and 35 were tested for their ability to activate PPARα, *in*

vitro. Compound 33 was very effective at activating PPARα from 1-100 μM, but compound 31, which is structurally similar to compound 33, was minimally effective at only the 10 μM dose and not effective at either 1 or 100 μM. One of ordinary skill in the art at the time the invention was made would not be able to predict which derivative of formula I would be effective for the treatment or prophylaxis of the claimed pathologies.

Despite the great deal of evidence presented by Applicant, the state of the prior art does not currently accept that a class of compounds is capable of treating every claimed pathology or disease nor capable of preventing every claimed pathology or disease. Even Applicant's own cited bibliography tends to show evidence of the treatment of specific pathologies rather than their prevention. Because of the aforementioned reasoning, Claims 38-67 are rejected, and one suggestion to overcome this rejection is to delete the word "prophylaxis" from Claims 38-67.

Claim Rejections - 35 USC § 112 (2nd paragraph)

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 38-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. The rejected claims recite "composition for the treatment or prophylaxis of a pathology related to....." These compounds are not being evaluated for therapeutic utility and only the composition is being evaluated here. Functional language as that of the instant claims carries no patentable weight in claims for compositions of matter see *Union Oil Co. of California v.*

Atlantic Richfield Co. 54 USPQ2d 1227 where "composition claims cannot, as the appellant refiners argue, embrace only certain uses of that composition. (citing *In Re Spada*) Otherwise these composition claims would mutate into method claims." It is unclear if these are method claims or a composition claims, based on the election these must be compound claims. It is recommended that these claims be canceled or rewritten with the removal of the intended use recitation.

14. The rejected claims recite that "at least one of the groups of X1, X3, X4, or X5 corresponding to the formula –G-R . . ., and with at least one of the groups R1, R3, R4, or R5 present in the form of an alkyl group containing at least one substituent from group 1 or 2, said alkyl group being bound directly to the ring or being associated with a group G according to the formula –GR." Neither the specification nor the claims define what is meant by "associated with" nor what -G or –R can be. It is unclear what Applicant is claiming as their invention, therefore, the rejected claims are considered indefinite.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 38-40, 42, 44, 46-48, 56, 58, 63-65, and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vanstone, et al. (US Patent No. 4,190,671, 1980, provided in Requirement for Restriction/Election mailed on 06/27/2008).

18. Claims 38 and 39 of the instant application are drawn to a composition comprising a derivative of formula I, with the exception of a derivative wherein X_2 is –H, and X_1 is $-G_1R_1$ wherein G_1 is -O- and R_1 is $-CH_2COOH$. Claims 40, 42, 44, 46-48, 56, and 58 limit the substituents of formula I. Claims 63-65 and 67 are drawn to a compound with an intended use of the compound for treatment. Examiner respectfully notes that statements of intended use do not limit the scope of the rejected claims. "If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction. *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999)." (MPEP § 2111.02)

19. Vanstone, et al., teach a derivative of formula I wherein X_2 is –H, and X_1 is $-G_1R_1$ wherein G_1 is -O- and R_1 is $-CH_2COOH$ (Example 22, col 16, line 19). An embodiment of the claimed derivative of formula I is 4'-carboxyethoxy-4-sulphochalcone, wherein:

X_1 = $-G_1R_1$, wherein G_1 is -O- and R_1 is $-CH_2CH_2COOR_6$ (group 1), wherein R_6 is –H;
X_2 = -H;

X_3 = -R_3, wherein R_3 is –H;
X_4 = -SO_3H;
X_5 = -R_5, wherein R_5 is-H; and,
X_6 = -O

The only difference between this embodiment and that taught by Vanstone, et al., is R_1 in Vanstone is CH_2COOH, while the compound in the claimed embodiment, R_1 is CH_2CH_2COOH. Both the compositions taught are useful for treating inflammation (Vanstone, et al., abstract, and instant specification, pg 2, lines 18-20). Absent evidence to the contrary, homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH_2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977) (MPEP § 2144.09). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the composition taught by Vanstone by adding the additional -CH_2- group to R_1.

Double Patenting

20. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

21. Claims 38, 61, and 62 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim1, 5, and 10, respectively of copending Application No.

11/493,040. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

22. Claims 38, 39, 61, and 62 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 69, 70, 96, and 97, respectively of copending Application No. 10/520,079. The rejection is statutory because Applicant has elected the same group (wherein X_2 is –H) in both the instant application and the copending '079 application. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

23. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

24. Claim 38 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 7,385,082. Although the conflicting claims are not identical, they are not patentably distinct from each other because Claim 1 of the '082 patent is drawn to a method of preparing a 1,3-diphenylprop-2-en-1-one whereas Claim 38 of the instant application is drawn to the compound made by the claimed method in the '082 patent.

Conclusion

25. No claims are allowed.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL ZAREK whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, PATRICK NOLAN can be reached on (571) 272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/Patrick J. Nolan/
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